

## Amendments to the Claims

In accordance with 37 CFR 1.121 a Claim Listing is included and the status of each claim is indicated according to the seven permissible status identifiers, i.e. (Original), (Currently amended), (Cancelled), (Previously presented), (New), (Not entered), (Withdrawn). Amended claims use underline for additions and ~~strike-through~~ for deletions.

### Claim Listing:

Claim 1. (currently amended) A combination therapeutic and diagnostic microparticle comprising a core, at least one linking carrier on said core, wherein said linking carrier comprises a biocompatible polymer, and at least two ~~one~~ radioactive therapeutic agents ~~agent~~ covalently bonded to said linking carrier; wherein said microparticle has a diameter in the range of from 5 to 200 microns and said microparticle is non-biodegradable and is not water swellable, wherein the at least two radioactive therapeutic agents are selected from the group consisting of a therapeutic beta-emitting radionuclide and an imaging or diagnostic gamma-emitting radionuclide.

Claim 2-7. (canceled).

Claim 7. (currently amended) The microparticle of claim 1 ~~particle of claim 5~~, wherein said radioactive therapeutic agent is at least one radionuclide selected from the group consisting of iridium, radium, cesium, phosphorus, yttrium, rhenium, actinium, bismuth, astatine, technetium, indium, iodine, and carbon, nitrogen, fluorine, sodium, magnesium, aluminum, silicon, potassium, vanadium, manganese, gallium, niobium, iodine, lead, Y-90, Bi-213, At-211, I-123, I-125, I-131, At-211, Cu-67, Sc-47, Ga-67, Rh-105, Pr-142, Nd-147, Pm-151, Sm-153, Ho-166, Gd-159, Th-161, Eu-152, Er-171, Re-186, Re-188, Tc-99m, In-111, Ga-67, Rh-105, I-123, Nd-147, Pm-151, Sm-153, Gd-159, Th-161, Er-171, Re-186, Re-188, and Tl-201.

Claim 8. (currently amended) The microparticle ~~particle~~ of claim 1, wherein said therapeutic beta-emitting radionuclide ~~radioactive therapeutic agent~~ is yttrium-90.

Claim 9-10. (canceled)

Claim 11. (currently amended) The microparticle of claim 1 ~~particle of claim 10~~, wherein said therapeutic beta-emitting radionuclide is yttrium-90 and said ~~an~~ imaging or diagnostic gamma-emitting radionuclide is selected from the group consisting of indium-111 and Tc-99m.

Claim 12. (currently amended) The microparticle of claim ~~particle of claim 1~~, wherein said radioactive therapeutic agent is bonded to said linking carrier through one or more spacer groups.

Claim 13. (currently amended) The microparticle of claim particle of claim 1, wherein said radioactive therapeutic agent is bound to said linking carrier by a chelator group.

Claim 14. (currently amended) The microparticle of claim particle of claim 13, wherein said chelator group is at least one selected from the group consisting of cyclohexyldiethylenetriaminepentaacetic acid ligand (CHX-DTPA), diethylenetriaminepentaacetic acid (DTPA), ethylenediaminetetraacetic acid (EDTA), 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetate (DOTA), tetraazacyclotetradecane-N,N'',N'''-tetraacetic acid (TETA), cyclohexyl 1,2-diamine tetra-acetic acid (CDTA), ethyleneglycol-O,O'-bis(-2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic acid (TTHA), hydroxyethyldiamine triacetic acid (HEDTA), hydroxyethylidene diphosphonate (HEDP), dimercaptosuccinic acid (DMSA), diethylenetriaminetetramethylenephosphonic acid (DTTP) and 1-(p-aminobenzyl)-DTPA, 1,6-diamino hexane-N,N,N',N'-tetraacetic acid, DPDP, and ethylenebis(oxyethylenenitrilo)-tetraacetic acid.

Claim 15. (currently amended) The microparticle of claim 13 ~~particle of claim 13~~, wherein said therapeutic beta-emitting radionuclide ~~radioactive therapeutic agent~~ is yttrium-90 and said chelator group is DOTA.

Claim 16. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said core is non-ceramic and non-radioactively labeled.

Claim 17. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said core comprises a polymer selected from the group consisting of polyacrylate, ethylene-vinyl acetate polymer, an acyl substituted cellulose acetate, polyurethane, polystyrene, polyvinylchloride, polyvinyl flouride, poly(vinyl imidazole), chlorosulphonate polyolefin, polyethylene oxide, blends thereof, and copolymers thereof, a polyphosphazine, a poly(vinyl alcohol), a polyamide, a polycarbonate, a polyalkylene, a polyacrylamide, a polyalkylene glycol, a polyalkylene oxide, a polyalkylene terephthalate, a polyvinyl ether, a polyvinyl ester, a polyvinyl halide, polyvinylpyrrolidone, a polyglycolide, a polysiloxane, and copolymers thereof, a alkyl cellulose, an hydroxyalkyl cellulose, a cellulose ether, a cellulose ester, and a nitrocellulose.

Claim 18. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said at least one linking carrier is selected from the group consisting of a linear polymer, a branched polymer, and a dendromer polymer.

Claim 19. (currently amended) The microparticle of claim 18 ~~particle of claim 18~~, wherein said at least one linking carrier is a dendrimer.

Claim 20. (currently amended) The microparticle of claim 19 ~~particle of claim 19~~, wherein said dendrimer has a disulfide bond in its core.

Claim 21. (currently amended) The microparticle of claim 19 ~~particle of claim 19~~, wherein said dendrimer has a final external layer which is capped with a reactive group.

Claim 22. (currently amended) The microparticle of claim 21 ~~particle of claim 21~~, wherein said reactive group is an amine or carboxyl group.

Claim 23. (currently amended) The microparticle of claim 21 ~~particle of claim 21~~, wherein said reactive group is derivatized with at least one selected from the group consisting of a targeting entity and a therapeutic entity.

Claim 24. (currently amended) The microparticle of claim 19 ~~particle of claim 19~~, wherein said dendrimer has a terminal functional group which is accessible to a chelate containing compound which is capable of interacting with the functional groups.

Claim 25. (currently amended) The microparticle of claim 24 ~~particle of claim 24~~, wherein said functional group is at least one selected from the group consisting of ester group, ether group, thiol group, carbonyl group, hydroxyl group, amide group, carboxylic group, and imide group.

Claim 26. (currently amended) The microparticle of claim 19 ~~particle of claim 19~~, comprising multiple dendrimers, wherein said dendrimers are monodispersed.

Claim 27. (withdrawn as non-elected species). The particle of claim 18, wherein said linking carriers are linear polymers.

Claim 28. (withdrawn as non-elected species). The particle of claim 1, wherein said radioactive therapeutic agent is covalently bonded to said linking carrier via a bifunctional linker, carbodiimide condensation, or a disulfide bond formation.

Claim 29. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said particle does not leach radionuclide.

Claim 30. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said particle is spheroidal.

Claim 31. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said particle has a density in the range of from 1 to 4 gm/cm.<sup>sup.3</sup>.

Claim 32. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said particle has a density in the range of from 1 to 2 gm/cm.<sup>sup.3</sup>.

Claim 33. (currently amended) The microparticle of claim 1 ~~particle of claim 1~~, wherein said particle further comprises a second therapeutic agent or a diagnostic agent.

Claim 34. (currently amended) The microparticle of claim 33 ~~particle of claim 33~~, wherein said second therapeutic agent or said diagnostic agent is at least one selected from the group consisting of a metal chelate complex, a drug, a prodrug, a radionuclide, a boron addend, a labeling compound, a toxin, a cytokine, a lymphokine, a chemokine, an immunomodulator, a radiosensitizer, an asparaginase, a radioactive halogens, a chemotherapy drug and a contrast

agent.

Claim 35. (currently amended) A particulate material comprising microparticles having: a core, at least one linking carrier on said core, wherein said linking carrier comprises a biocompatible polymer, and at least two radioactive therapeutic agents covalently bonded to said linking carrier; wherein said microparticle has a diameter in the range of from 5 to 200 microns and said microparticle is non-biodegradable and is not water swellable, wherein the at least two radioactive therapeutic agents are selected from the group consisting of a therapeutic beta-emitting radionuclide and an imaging or diagnostic gamma-emitting radionuclide. ~~at least one radioactive therapeutic agent covalently bonded to said linking carrier; wherein said microparticles have a diameter in the range of from 5 to 200 microns and said microparticles are non-biodegradable.~~

Claim 36. (original) The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 8-100 microns.

Claim 37. (original) The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 25-50 microns.

Claim 38. (original) The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 20-30 microns.

Claim 39. (original) The particulate material of claim 35, wherein said microparticles have substantially equivalent particle sizes.

Claim 40. (original) The particulate material of claim 35, wherein said microparticles are sufficiently large so as to avoid phagocytosis.

Claim 41. (withdrawn as non-elected invention) A method of radiation therapy of a patient, which comprises administering to the patient at least one of the microparticles of claim 1, or the particulate material of claim 35, ~~wherein said microparticles comprise~~

~~— a core,~~

~~— at least one linking carrier on said core, wherein said linking carrier comprises a biocompatible polymer, and~~

~~— at least one radioactive therapeutic agent covalently bonded to said linking carrier;~~

~~— wherein said microparticle has a diameter in the range of 5 to 200 microns and said microparticle is non-biodegradable.~~

Claim 42. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said microparticles are administered internally.

Claim 43. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein the administration is direct to a lesion or through a vascular route.

Claim 44. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats cancer or a tumor.

Claim 45. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 44, wherein said cancer is primary or secondary cancer of the liver.

Claim 46. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats a highly vascularized tumor or a tumor which has a single dominant arterial vascular supply.

Claim 47. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 46, wherein said microparticles are injected into an artery supplying a tumor.

Claim 48. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats hepatic cancer, rheumatoid arthritis, a solid cancer, liver cancer, brain cancer, breast cancer and/or ovary cancer.

Claim 49. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats renal cell carcinoma, hepatoma, sarcomas, cancer of the head or neck, and/or a central nervous system tumor.

Claim 50. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said at least one radioactive therapeutic agent is at least one radionuclide selected from the group consisting of an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

Claim 51. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 50, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide and a beta-emitting radionuclide.

Claim 52. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 51, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

Claim 53. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, comprising radiation treatment and imaging or diagnosing.

Claim 54. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 53, wherein said imaging or diagnosing is during the life of the radiation.

Claim 55. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 53, wherein said imaging or diagnosing is post life of the radiation.

Claim 56. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 51, further comprising assaying the gamma radiation to determine the location of the microparticles in the patient.

Claim 57. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said particles are immobilized at a site of administration.

Claim 58. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said particles do not release a significant amount of radiation emitting radioisotope into the circulation system upon administration.

Claim 59. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said particles have a diameter of from 15 to 35 microns.

Claim 60. (withdrawn as non-elected invention) A kit for preparing a microparticle treatment dose for a patient in need thereof wherein said treatment dose comprises the particulate material of claim 35, wherein said kit comprises

particle cores, which do not comprise radionuclide,

linkers for attaching at least one radionuclide to said particle cores, and

instructions or a means for obtaining instructions for preparing said microparticle treatment dose.

Claim 61. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, wherein said kit contains a radionuclide.

Claim 62. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, wherein a radionuclide is provided separately from said kit.

Claim 63. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, further comprising at least one component selected from the group consisting of an inert pharmaceutically acceptable carrier, a formulating agent, an adjuvant, an active agent, water, saline, a transfer ligand, a reducing agent, a lyophilization aid, a stabilization aid, a solubilization aid, a bacteriostat, a buffer, an X-ray contrast agent, an ultrasound contrast agent, and a metallopharmaceutical.

Claim 64. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, further comprising at least one component selected from the group consisting of a syringe, shielding, and imaging equipment.

Claim 65. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, wherein said kit comprises multiple types of cores and multiple types of linkers.

Claim 66. (withdrawn as non-elected invention) A method of using the kit of claim 60 to prepare a microparticle treatment dose for a patient in need thereof,

determining the type and dosimetry of microparticle treatment needed from a prescription for said patient and preparing said microparticle treatment dose from said instructions or said means for obtaining instructions.

Claim 67. (withdrawn as non-elected invention) A method of using the kit of claim 60 to prepare a microparticle treatment dose for a patient in need thereof,

determining the type and dosimetry of microparticle treatment needed from a prescription for said patient,

selecting a type of core from the cores included in said kit,

selecting a type of linker from the linkers included in said kit,

selecting a radionuclide and

preparing said microparticle treatment dose from said instructions or said means for obtaining instructions.

Claim 68. (withdrawn as non-elected invention) The method of claim 60, wherein said microparticle treatment dose is made said kit at a location of administration or at a site proximate to the location of administration.

Claim 69. (withdrawn as non-elected invention) The method of claim 60, wherein said location or said site is a local radiopharmacy, laboratory, hospital or physician's office.

Claim 70. (withdrawn as non-elected invention) The method of claim 60, wherein said microparticle treatment dose are made said kit at a location of administration or at a site proximate to the location of administration.

Claim 71. (withdrawn as non-elected invention) The method of claim 60, wherein said location or said site is a local radiopharmacy, laboratory, hospital or physician's office.

Claim 72-81. (canceled)

Claim 82 (withdrawn as non-elected invention). A method of radiation therapy of a patient, which comprises administering to the patient microparticles, wherein said microparticles comprise the microparticle as claimed in claim 72.

Claim 83 (withdrawn as non-elected invention). The method of radiation therapy of a patient of claim 82, comprising radiation treatment and imaging or diagnosing.

Claim 84 (withdrawn as non-elected invention). The method of radiation therapy of a patient of claim 82, further comprising assaying the gamma radiation to determine the location of the microparticles in the patient.

85. (currently amended) The microparticle ~~particle~~ of claim 1, wherein said microparticle has a diameter in the range of from about 8 to about 100 microns.

86. (currently amended) The microparticle ~~particle~~ of claim 1, wherein said microparticle has a diameter in the range of from about 20 to about 30 microns.